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PATENT

Attny. Docket No. DIV-1460-15

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Jay M. Short Examiner: H. Park  
U.S. Serial No. 09/594,459 Art Unit: 1648  
Filing Date: June 14, 2000

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For: **SYNTHETIC LIGATION REASSEMBLY IN  
DIRECTED EVOLUTION**

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Dec. 23, 2002  
Date

Nancy E. Gilmore  
Nancy E. Gilmore

Hon. Commissioner for Patents  
Washington D.C. 20231

Dear Sir:

**COMMUNICATION IN REPLY TO AUGUST 5, 2002 OFFICE ACTION AND  
PETITION FOR A TWO-MONTH EXTENSION OF TIME**

This Communication is submitted in reply to the August 5, 2002 Office Action which was issued by the U.S. Patent and Trademark Office in connection with the above-identified application. A response was originally due November 5, 2002 and applicant hereby requests a two-month extension of time to January 5, 2003. Thus, this Communication is being timely filed.

Claims 3-14 are pending.

**Rejection of Claims 3-14 Under 35 U.S.C. § 103**

The Examiner rejected claims 3-14 as being obvious in view of PCT Publication No. WO 00/42560, Selifonov, et al. The Examiner stated that it would have been obvious to use Selifonov's method to obtain a progeny library with predetermined polynucleotide sequences comprising non-stochastically assembling nucleic acid building block sequences to produce the chimerized but pre-determined polynucleotide sequences. The Examiner references page 9, lines 23-26 and pp 18-66.

In reply, applicant traverses the rejection and maintains that the claimed methods are not rendered obvious by Selifonov et al. Claim 3 of the subject application is directed to a method of producing a progeny library comprised of chimerized but pre-determined polynucleotide sequences each of which is comprised of a pre-determined number of building block sequences that are assembled in non-random order, the method comprising: (a) generating a plurality of pre-determined nucleic acid building block sequences comprised of sequences delineated by demarcation points

selected from aligned progenitor nucleic acid sequences; and (b) non-stochastically assembling said nucleic acid building block sequences to produce said chimerized but pre-determined polynucleotide sequences, such that a designed overall assembly order is achieved for each of said chimerized but pre-determined polynucleotide sequences. Claims 4-14 all depend from claim 3. Selifonov et al. do not teach or suggest the non-stochastic method of producing a progeny library as set out above.

On the contrary, Selifonov et al. describe general random methods of recombination. For example, on page 21, Selifonov et al. describe an embodiment of the disclosed method:

When recombining homologous nucleic acids, sets of overlapping family gene shuffling oligonucleotides (which are derived by comparison of homologous nucleic acids and synthesis of oligonucleotide fragment sets, which correspond to regions of similarity and regions of diversity derived from the comparison) are hybridized and elongated (e.g., by reassembly PCR), providing a population of recombined nucleic acids, which can be selected for a desired trait or property.

Selifonov et al. do not teach or render obvious generating a plurality of "pre-determined nucleic acid building block sequences" as recited in the pending claims, but rather describe the production of "fragments" which are allowed to randomly overlap

with other fragments via the recombination methods disclosed ("DNA shuffling") to produce recombinant nucleic acids. See Selifonov et al., page 22, ¶ 1-2.

Selifonov et al. do not teach or make obvious the step of "non-stochastically assembling said nucleic acid building block sequences" as set forth in step (b) of claim 3.

Selifonov et al. set out five different "general classes of recombination methods" that can be used (see pp 28-29) and none of the methods include non-stochastic assembly of nucleic acid building blocks as required by the claimed invention. Indeed, the Selifonov et al. methods include the step of "allowing recombination to occur between the nucleic acids..." which indicates that the step is homology-based rather than non-stochastic.

For example, there is no disclosure or suggestion by Selifonov et al. of a "designed overall assembly order" as required by step (b) of claim 3.

Accordingly, since there is no teaching or disclosure of the non-stochastic aspects of the claimed invention, one of ordinary skill in the art would have no expectation of success in carrying out the claimed methods to produce a progeny library comprised of chimerized but pre-determined polynucleotide sequences by following the teaching of Selifonov et al.

Thus, applicant requests the Examiner to reconsider and withdraw this ground of rejection.

**Conclusion**

If a telephone interview would be of assistance in advancing the prosecution of the above-identified application, applicant's undersigned attorney invites the Examiner to telephone her at the number provided below.

Authorization is hereby given for the deduction of the fee of **\$200.00** from Deposit Account No. 08-0219 for the two-month extension of time. Additionally, please charge any additional fees which may be due, or credit any overpayment to Deposit Account No. 08-0219.

Date: 12/23/02

Respectfully submitted,

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